fragments were synthesized: PCR1 of 465 bp (primer 1: (SEQ ID NO:4) 5'-CCC CCC GGG CCA CCA TGG TTT TTT CAA CAC CAA TTC CAT TTT CTT ATT C-3' and primer 2: (SEQ ID NO: 5) 5'-CTA AAC CAG TAA TTT CTG-3'), PCR2 of 648 bp (primer 3: (SEQ ID NO:6) 5'-AAT TAT GGA CTT TAA AAG ATT CCG C-3' and primer 4: (SEQ ID NO: 7) 5'-GGC ATT ATA ACC TAC TCT TAG AAT-3') and PCR3 of 338 bp (primer 5: (SEQ ID NO: 8) 5'-AAT GCC TTT AAT AAT CTT GAT AGA AAT-3' and primer 6: (SEQ ID NO: 9) 5'-CCC CCC GGG CAT ATG TCA TGA ACA TAT CAA TCT GTT TAA TC-3'). The three fragments were sequentially introduced into pBluescript KS+ (Stratagene) to give pBS:TTC plasmid. The upstream primer 1 also contains an optimized eukaryotic Ribosome Binding Site (RBS) and translational initiation signals. Our TTC fragment (462 amino acids) represents the amino acids 854-1315 of tetanus holotoxin, i.e. the carboxy-terminal 451 amino acids of the heavy chain, which constitute the fragment C plus 11 amino acids of the heavy chain that immediately precede the amino terminus of the fragment C. The DNA sequence and amino acid sequence of the TTC fragment cloned in pBS:TTC is shown in Figure 1. The construct pBS:TTC is shown in Figure 2.

Page 20, second paragraph, beginning at line 15 through page 21, line 2, please replace with the following paragraph:

pGEX:*lacZ* was obtained by cloning a *SmaI/XhoI lacZ* fragment from the pGNA vector (a gift from Dr. H. Le Mouellic) into pGEX 4T-2 (Pharmacia). PCR was used to convert the *lacZ* stop codon into an *NcoI* restriction site. Two primers (upstream: (SEQ ID NO: 12) 5'-CTG AAT ATC GAC GGT TTC CAT ATG-3' and downstream: (SEQ ID

LAW OFFICES
FINNEGAN, HENDERSON,
FARABOW, GARRETT,
& DUNNER, L.L.P.
1300 I STREET, N. W.
WASHINGTON, DC 20005
202-408-4000

NO: 13) 5'-GGC AGT CTC GAG TCT AGA CCA TGG CTT TTT GAC ACC AGA C-3') were used to amplify the sequence between *NdeI* and *XhoI*, generating pGEX:*lacZ(NcoI)* from pGEX:*lacZ*. pGEX:*lacZ*-TTC was obtained by insertion of the TTC *NcoI/XhoI* fragment into pGEX:*lacZ(NcoI)*, fusing TTC immediately downstream of the *lacZ* coding region and in the same reading frame. Figure 3 shows the details of the pGEX:*lacZ*-TTC construct.

Page 21, the paragraph beginning at line 4, please replace with the following paragraph:

pBS:TTC was modified to change *NcoI* into a *BamHI* restriction site (linker (SEQ ID NO: 14) 5'-CAT GAC TGG GGA TCC CCA GT-3') at the start of the TTC DNA, to give pBS:TTC*(BamHI)* plasmid. pGEX:TTC was obtained by cloning The TTC *BamHI/SmaI* fragment from pBS:TTC*(BamHI)* into pGEX 4T-2 (Pharmacia). PCR was used to convert the TTC stop codon into an *NheI* restriction site. Two primers (upstream: (SEQ ID NO: 15) 5'-TAT GAT AAA AAT GCA TCT TTA GGA-3' and downstream: (SEQ ID NO: 16) 5'-TGG AGT CGA CGC TAG CAG GAT CAT TTG TCC ATC CTT C-3') were used to amplify the sequence between *NsiI* and *SmaI*, generating pGEX:TTC*(NheI)* from pGEX:TTC. The lacZ cDNA from plasmid pGNA was modified in its 5' extremity to change *SacII* into an *NheI* restriction site (linker 5'-GCT AGC GC-3'). pGEX:TTC-*lacZ* was obtained by insertion of the *lacZ NheI/XhoI* fragment into pGEX:TTC*(NheI)*, fusing *lacZ* immediately downstream of the TTC coding region and in

LAW OFFICES
FINNEGAN, HENDERSON,
FARABOW, GARRETT,
& DUNNER, L.L.P.
1300 I STREET, N. W.
WASHINGTON, DC 20005
202-408-4000

the same reading frame. The details of the construct of pGEX:TTC-*lacZ* are shown in Figure 4.

Page 21, paragraph beginning at line 21 through page 22, line 2, please replace with the following:

pCMV vector was obtained from pGFP-C1 (Clontech laboratories) after some modifications: GFP sequence was deleted by a *BglII/NheI* digestion and religation, and *SacII* in the polylinker was converted into an *AscI* restriction site (linkers 5'-GAT ATC GGC GCG CCA GC-3' (SEQ ID NO: 17) and (SEQ ID NO: 18) 5'-TGG CGC GCC GAT ATC GC-3').

Page 22, second paragraph, beginning at line 3 through line 14, replace with the following paragraph:

pBluescript KS+ (Stratagene) was modified to change *XhoI* into an *AscI* restriction site (linker (SEQ ID NO: 19) 5'-TCG ATG GCG CGC CA-3'), giving pBS*(AscI)* plasmid. pBS:*lacZ*-TTC was obtained by cloning a *XmaI lacZ*-TTC fragment from pGEX:*lacZ*-TTC into pBS*(AscI)*. pCMV:*lacZ*-TTC was obtained by insertion of the *lacZ*-TTC *XmnI/AscI* fragment into pCMV vector at the *XhoI* and *AscI* sites (*XhoI* and *XmnI* was eliminated with the clonage), putting the fusion downstream of the CMV promotor. Figure 8 shows the details of the construct pCMV:*lacZ*-TTC. Plasmid pCMV:*lacZ*-TTC was deposited on August 12, 1997, at the Collection Nationale de Cultures de Microorganisms (CNCM), Institut Pasteur, 25, Rue du Docteur Roux, F-75724, Paris Cedex 15, France, under Accession No. I-1912.

LAW OFFICES
FINNEGAN, HENDERSON,
FARABOW, GARRETT,
& DUNNER, L.L.P.
1300 I STREET, N.W.
WASHINGTON, DC 20005
202-408-4000